REMARKS

STATUS OF THE CLAIMS

Claims 24-70 were pending as shown in the paper filed May 24, 2004. Pursuant to a Restriction Requirement (discussed below) that has now been made FINAL, claims 30, 31 and 43 have been withdrawn from consideration.

By virtue of this Response, claims 25, 26, 34, 40, 44-47 and 51-70 have been canceled, without prejudice or disclaimer, and the dependencies of claims 30, 32, 43 and 48 have been amended in light of the cancellation of claim 25. The dependencies of claims 27-29 have been amended in light of the cancellation of claim 26. Claims 41 and 42 have been amended to change their dependencies in light of the cancellation of claim 40. The dependency of claim 38 has been amended so that proper antecedent basis is present.

Claim 24 has been amended as shown above to make explicit what was previously implicit, namely that the zinc finger polypeptide is not simply genetically engineered, but engineered to bind to the target DNA sequence. Support for this amendment can be found throughout the specification as filed, for example, page 3, lines 15-17; page 3, lines 19-22 and page 4, line 22 through page 5, line 3. Claim 24 has also been amended to make explicit that the binding motif of the zinc finger(s) making up the zinc finger polypeptide comprises SEQ ID NO:22, as described, for example, on page 11 of the specification and in previous claim 26.

Claim 48 has been amended to replace the term "biological effector domain" with "catalytic domain of a restriction enzyme." Support is found, for example, at page 40, lines 8-10.

New claim 71 has been added to recite an embodiment previously recited in canceled claim 25. Support is found in original claim 25 and at page 12, lines 4-6.

Accordingly, claims 24, 26-33, 35-39, 41-43, 48-50 and 71 are pending as shown above and claims 24, 26-29, 32, 33, 35-39, 41, 42, 48-50 and 71 are under consideration.

Inasmuch as the aforementioned amendments are believed to simplify issues for appeal by providing explicit recitation of the claimed subject matter, reducing the number of claims and correcting dependencies, entry thereof is respectfully requested if the finality of the Office Action is maintained.

REQUEST TO WITHDRAW FINALITY

The outstanding Office Action was made FINAL on the grounds that Applicants amendments necessitated the new grounds of rejections. However, no amendments were made in the last-filed paper, which was solely a Response to Restriction Requirement.

Moreover, the most recent amendments to the claims, made in a paper filed May 24, 2004, simply added sequence identifiers. Since these amendments cannot possibly necessitate new grounds of rejection, Applicants request that finality be withdrawn so that the issues presented may be fully addressed.

RESTRICTION REQUIREMENT

The Restriction Requirement has been made FINAL. Applicants' grounds for traversal were all deemed unpersuasive. Applicants reiterate, and incorporate by reference herein, the arguments previously presented. Applicants reserve the right to petition the present Final Restriction Requirement at any time during the pendency of this application.

35 U.S.C. § 112, 1ST PARAGRAPH, WRITTEN DESCRIPTION

All examined claims stand rejected under 35 U.S.C. § 112, 1st paragraph as allegedly not described by the specification as filed. In support of the rejection, the Final Office Action stated (paragraph bridging pages 5-6):

> ...the Examiner maintains that Applicant's disclosure of the state of the art with respect to zinc finger polypeptides does not serve to describe what Applicants have invented. In this regard, the Examiner maintains that Applicants' description of a plant host cell or transgenic plant comprising a polynucleotide of SEQ ID NO:4 ... does not constitute an adequate description of a substantial portion of the claimed genus that encompasses plant cells and plants comprising polynucleotides encoding any unspecified zinc finger polypeptide engineered in any unspecified manner and any unspecified target DNA sequence to which the zinc finger polypeptide binds, plant cells and plants comprising polynucleotides

> encoding zinc finger polypeptides having any unspecified combination of two or more, more than three ... four, five, six, even, eight or nine zinc fingers of the formula [omitted].
>
> The Examiner also maintains that evincing possession of the claimed subject matter by Applicants is not the sole test for whether there is an adequate description [citing and quoting *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609, 1617].

Simply put, it was alleged that the genus encompassed by the claims is not described by the specification as filed.

Because the specification as filed clearly describes the subject matter of the pending claims, and to the extent that the foregoing amendments do not obviate this rejection, Applicants traverse the rejection and supporting remarks.

The Examiner's assertion that establishing possession of the invention is not the sole test for description is not accurate and not supported by citation to *Enzo Biochem Inc.*. In fact, it is well-settled law that fundamental factual inquiry in written description is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. *See, e.g., Vas-Cath, Inc.*, 935 F.2d at 1563-64, 19 USPQ2d at 1117. Determining whether the written description requirement is satisfied is a question of fact and the burden is on the Examiner to provide evidence as to why a skilled artisan would not have recognized that the applicant was in possession of claimed invention at the time of filing. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim,* 191 USPQ 90 (CCPA 1976). It is not necessary that the application describe the claimed invention *in ipsis verba.* Rather, all that is required is that the specification reasonably convey possession of the invention. *See, e.g., In re Lukach,* 169 USPQ 795, 796 (CCPA 1971). Finally, determining whether the written description requirement is satisfied requires reading the disclosure in light of the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lange,* 209 USPQ 288 (CCPA 1981).

The Patent Office's own guidelines on written description, which the Federal Circuit in *Enzo* commented favorably upon, are in accord -- the written description requirement may be met by showing possession. In addition, the Guidelines stress that the written description requirement is highly fact-dependent and that there is a strong presumption that an adequate written description of the claimed invention is present at the time of filing:

> [t]he description need only describe in detail that which is new or not conventional. This is equally true whether the claimed invention is a product or a process. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that the applicant was in possession of the claimed invention, i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with known or disclosed correlation between function and structure, or some combination of such characteristics.
> (Final Examiner Guidelines on Written Description, 66 Fed. Reg. 1099, emphasis added).

Thus, and contrary to the statements in the Final Office Action, the Patent Office has determined that possession is in fact the proper test for determining adequate description and, moreover, the Federal Circuit in *Enzo Biochem* commented favorably on the use of the possession test as set forth in the Guidelines. See, Appendix A, a copy of slides presented by Dr. Stephen Walsh at the meeting held on June 7, 2005.[1]

These guidelines, which the *Enzo* court found to be helpful in determining whether the written description requirement is satisfied, include Examples that show that description of a broad genus can be present when only one representative species is present. Indeed, PTO Example 14 entitled "product-by-function" reads, in part, as follows:

> **Claim**:
> A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A⟶ B.
>
> **Analysis:**
> ... The procedures for making variants of SEQ ID NO:3 are conventional in the art and an assay is described which will identify other proteins having the

[1] Since the meeting at which this presentation was made was not held until June 7, 2005, these slides could NOT have been earlier presented. Thus, good and sufficient reasons have been presented as to why this evidence is now submitted.

> claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art. ....
>
> There is actual reduction to practice of a single disclosed species. The specification indicates that the genus of proteins that must be variants of SEQ ID NO:3 does not have substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO:3. The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity. One of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus.
>
> **Conclusion:** The disclosure meets the requirements of 35 U.S.C. § 112, first paragraph as providing adequate written description for the claimed invention.

The claim, analysis and conclusion set forth in PTO Example 14 are directly relevant and analogous to the written description analysis in the pending case. In particular, the pending claims are analogous to the "product by function" claim presented in PTO Example 14 in that they all recite a reference structure and include a function limitation (catalytic activity in PTO Example 14 and encoding a zinc finger polypeptide that has been engineered to bind to a target DNA sequence in the claims at issue).

Furthermore, as established by the Patent Office in the Guidelines, procedures for making variants of the sequences recited in the claims are utterly conventional in the art and are described in the pending application. Also conventional in the art and described in the specification are methods of engineering zinc finger polypeptides so that they bind to a target DNA sequence of choice.

Thus, actual reduction to practice of a single disclosed species is more than sufficient to satisfy the written description requirement in the case at hand because, as in PTO Example 14, sequences falling within the claimed genus must have the recited structure and function. Therefore, as in PTO Example 14, the genus encompassed by the pending claims is more than adequately described by the specification as filed. Put another way, a person having ordinary

skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus, and it is clear that, as concluded in PTO Example 14, the present specification provides adequate written description for the claimed subject matter.

Applying these standards to the case at hand, it is clear that, as acknowledged by the Office, Applicants have established that the skilled artisan would have recognized that they were in possession of the claimed subject matter at the time of filing. Accordingly, the written description requirement has been satisfied. There is absolutely **no** requirement that Applicants exemplify (or reduce to practice) every polynucleotide falling within the scope of the claims in order to adequately describe the claimed plants and cells. Rather, the test is whether the specification contains sufficient disclosure, regarding structural and functional characteristics of the molecules recited in the claims, to satisfy the written description requirement. For the reasons of record, the specification as filed, in view of the state of the art, more than adequately describes and details structure and function of the polynucleotides recited in the claims.

Indeed, since evaluating whether the written description requirement is satisfied requires, first and foremost, an evaluation of the scope of the claims (*i.e.*, the genus covered by the claims), the assertions that the claims contain "unspecified" variables are also in error. In reality, the pending claims do not have "unspecified" zinc finger polypeptides that are engineered in an "unspecified" manner or having an "unspecified" combination of binding motif-containing fingers. Rather, it is clearly specified that the zinc finger polypeptides include both the binding motif structure (SEQ ID NO:22) and, in addition, must be functional in that they bind to the target DNA sequence to which they have been engineered to bind. Therefore, the feature "engineered" is also clearly specified. Furthermore, the number of binding motifs is not unspecified, but clearly indicates that at least two zinc fingers having the recited binding motifs must be present.

Moreover, Applicants submit that the assertion that the sequence of the target DNA sequence must be specified in the claim in order for there to be adequate description is in error. Zinc finger polypeptide can be designed to bind to any target sequence of choice, as disclosed in

the specification; consequently, the target sequence, as recited in the claims, cannot be specified by a particular sequence. Indeed, to do so would be to prevent Applicants from claiming that which they believe to be one of their inventions. Thus, the fact that the target DNA sequence recited in the claims can vary, depending on the gene (or genes) whose expression is to be is modulated, in no way supports the contention that the specification does not adequately describe the pending claims.

In sum, all of the so-called "variables" of the claims are fully described in such a manner that the skilled artisan would have known that Applicants were in possession of the claimed subject matter at the time the specification was filed. The specification also contains a literal description of the claimed subject matter (*e.g.*, page 11 for SEQ ID NO:22). Thus, under either the proper "possession" test or the Examiner's literal description test, the specification describes the claimed subject matter.

Turning back to the *Enzo* decision itself, Applicants also submit that, given the fact-dependent nature of the written description inquiry, the particular quotation the Examiner has cited from *Enzo v. GenProbe* is not relevant to the case at hand. In *Enzo* the specification at issue lacked any description of the claimed molecules, and the issue was whether the applicant could rely on deposit of the claimed polypeptides to satisfy the written description requirement. In *Enzo* I (285 F.3d 1013 (Fed. Cir. 2002), the Federal Circuit held that deposit did not satisfy the written description requirement. However, within a few months, the court vacated its original opinion and reversed the result of *Enzo* I in *Enzo* II (323 F.3d 956, Fed. Cir. 2002). Thus, as show in Dr. Walsh's attached slides (Appendix A), *Enzo* explicitly rebuts the Examiner's contention that that possession is not the sole test for determining satisfaction of the written description requirement. Moreover, *Enzo* is clearly limited to disclosures in which the structure of the claimed molecules is not set forth in the specification (but inherent in the deposited material). Accordingly, both *Enzo* decisions are not germane to the case at hand.

Thus, for the reasons of record and the reasons and evidence presented herein, the claims as pending are fully described by the specification as filed and withdrawal of this rejection is in order.

35 U.S.C. § 112, 2ND PARAGRAPH

Claims 24[2], 25-29, 32-42 and 44-50 were again rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. Applicants address the rejections in turn.

Claim 24

The Office continues to object to the term "engineered" in claim 24, arguing that the polypeptides may be engineered in different ways, including cloning and other genetic engineering methods. Applicants have amended claim 24 as shown above to make explicit that the term "engineered" refers to a ZFP that has been engineered to bind to a target site. Thus, the claim clearly conveys what is meant by the term and withdrawal of the rejection is requested.

Claim 25

Claim 25 has been canceled, without prejudice or disclaimer. Accordingly, the rejections to this claim have been obviated.

Claims 26, 27 and 29

Claims 26, 27 and 29 were rejected as allegedly indefinite for the use of parentheses. In response, Applicants note that it is standard practice to isolate sequence identifiers with parentheses, and thus submit that the parentheses in these claims actually clarify the subject matter of the claims rather than rendering the claims indefinite. Accordingly, withdrawal of the rejection is requested.

Claims 28 and 32

Claims 28 and 32 were rejected as allegedly indefinite for the recitation "more than" in reference to the number of zinc fingers.

Applicant submits that the metes and bounds of the claims would be clear to one of ordinary skill in the art in view of the teachings of the specification. A claim that is clear to one ordinarily skilled in the art when read in light of the specification, does not fail for indefiniteness.

[2] Although the Final Office Action (page 6) indicates claim 1, Applicants assume the Office is referring to independent claim 24, as claim 1 was previously canceled.

Allan Archery, Inc. v. Browning Manufacturing Co., 819 F.2d 1087, 2 USPQ2d 1490 (Fed. Cir. 1987).

In reading claims 28 and 32, the skilled artisan would know that the zinc finger proteins could contain any number of zinc fingers. The notion that a skilled artisan would think the claims would encompass an "infinite" number of zinc fingers is untenable, as anyone working in this field would be well aware of the impossibility of this proposition and, more importantly, well aware from the language "more than" what the claims encompass. Therefore, the claims are definite because they would be clear to one of skill in the art.

Claim 48

Claim 48 was again rejected as allegedly indefinite for reciting "a biological effector domain." Without conceding the correctness of the Examiner's position and solely to advance prosecution, claim 48 has been amended as shown above to specify that the ZFP is fused to a catalytic domain of a restriction enzyme. Thus, the rejection may be withdrawn.

35 U.S.C. § 102

Claims 24, 35-36, 38, 39, 44 and 49-50 were again rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Aoyama.

The foregoing amendments to the claims obviate the rejection based on Aoyama. In particular, it is acknowledged by the Examiner that Aoyama does not describe or demonstrate ZFPs that have been engineered to bind a target DNA sequence, as claimed. Instead, Aoyama described a naturally occurring GAL4 ZFP that binds to a known target site. Since Aoyama's ZFP has not been engineered to bind to a target DNA sequence, this reference cannot anticipate the pending claims. Moreover, the GAL4 protein disclosed by Aoyama does not possess the structure defined by SEQ ID NO:22 that is set forth in claim 24. For these reasons, the rejection should be withdrawn.

Claims 24-25, 32-33, 35-37, 39, 44 and 46-50 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,534,261.

Independent claim 24 has been amended as shown above to incorporate the limitations of previous dependent claim 26. As the Examiner acknowledges, the subject matter of claim 26 (SEQ ID NO:22), which is now recited in independent claim 24, is a patentable species of the genus disclosed in U.S. Patent No. 6,534,261. Therefore, Applicants submit that the rejection has been obviated and request withdrawal thereof.

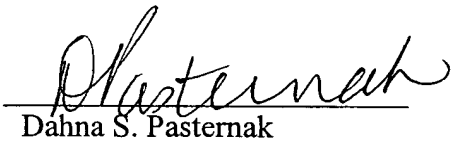
CONCLUSION

In view of the foregoing amendments, Applicants submit that the claims are now in condition for allowance and request early notification to that effect.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §1.16, §1.17, and §1.21, which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-1648, referencing Atty. Docket No. 2302-1631.20.

Respectfully submitted,

Date: June 27, 2005

By: 
Dahna S. Pasternak
Registration No. 41,411

ROBINS & PASTERNAK LLP
1731 Embarcadero Road, Suite 230
Palo Alto, CA 94303
Tel.: (650) 493-3400
Fax: (650) 493-3440

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Written Description Examination Guidelines

Stephen Walsh, Ph.D., J.D.
Associate Solicitor

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Examination Guidelines

- Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement
- 66 FR 1099 (Jan. 5, 2001)
- www.uspto.gov/web/offices/com/sol/notices/writdesguide.pdf

8

Written Description Standard

- To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had **possession** of the claimed invention.

9

Possession Tests

- Variety of ways such as
  - Actual reduction to practice
  - Show the invention was ready for patenting such as by the disclosure of drawings or structural chemical formulas showing the invention was complete
  - Describe distinguishing identifying characteristics sufficient to show possession
  - Other....

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What Are Distinguishing Identifying Characteristics?

- Complete or partial structure
- Other physical and/or chemical properties
- Functional characteristics when coupled with a known or disclosed correlation between function and structure
- Some combination of such characteristics

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USPTO Examiner Training Materials

- For examiner use, the Office prepared a "Synopsis of Application of Written Description Guidelines"
- These "training materials" are available at www.uspto.gov/web/menu/written.pdf

- Hybridization
- Antibodies
- Genus/species

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Hybridization

Example 9:

An isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO:1.

- Given the stringency conditions disclosed, the nucleic acid was adequately described
- A structure/function correlation

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Enzo Biochem Inc. v. Gen-Probe Inc., 323 F.3d 956 (Fed. Cir. 2002) (Enzo II)

Paraphrased Claim: A nucleic acid which hybridizes to *N. gonorrhoeae* chromosomal DNA under recited conditions.

- Reference to a deposit of a nucleotide sequence may adequately describe that sequence.
- Court vacated prior decision that patent for nucleic acid probes that selectively hybridize to genetic material of bacteria that cause gonorrhea did not comply with written description requirement.
- Are the deposited sequences representative of the scope of the genus claims? If so, they may indicate patentee has invented species sufficient to constitute the genus.

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Enzo (cont.)

- Decision included favorable commentary and discussion of the USPTO's Written Description Guidelines and examiner training materials.
- In this case, genuine issues of material fact exist regarding satisfaction of the written description requirement, thus summary judgment is inappropriate; district court's grant of summary judgment reversed and case remanded for further fact finding.

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Antibodies

- What Would Convince One Of Skill In the Art That An Inventor Was In Possession Of An Antibody?
  - Consider *Reiners v. Mehltretter*, 236 F.2d 418, 421 (CCPA 1956) ("the reactions to be obtained could, therefore, be predicted with a **reasonable** assurance of accuracy and under such circumstances it is not necessary that the proof of the identity of the products be as exhaustive as if entirely new substances or procedures were involved").

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Antibodies

Example 16: An isolated antibody capable of binding to antigen X.

- purified antigen X is described
- general knowledge of antibodies is they are structurally well characterized
- antibodies can be made against almost any protein
- the written description is adequate